In the Specification:

Please delete the Title of the Invention beginning at line 1 of the application and substitute therein the following title:

CHROMOSOME STRUCTURAL ABNORMALITY LOCALIZATION WITH SINGLE COPY PROBES

Please delete the two paragraphs beginning at page 24, line 17 to page 25, line 18 and replace them with the following two paragraphs:

Initially, a computer-based search using the search term "HIRA" was performed using Entrez Nucleotide software at the National Library of Medicine website. This identified a series of cDNA sequences for the HIRA gene in GenBank. The full length cDNA sequence was selected (GenBank Accession No. X81844), having 3859 bp. This cDNA sequence was then compared with the genome sequence which included draft sequences at the National Library of Medicine (ncbi.nlm.nih.gov/genome/seq/page.cgi?F=HsBlast.html&&ORG=Hs). This was done in order to determine whether genomic sequences of sufficient length were available for probe development. This comparison confirmed that the entire HIRA genomic sequence was known, and that the coding sequence interval spanned a length of 100,836 bp in the chromosome. Since the available contiguous genomic sequence in GenBank exceeded the length of the coding interval, it was possible to select an interval longer than the coding region in order to include

sequences from the gene promoter at the 5' end and untranslated sequences and polyadenylation signal at the 3' end. A total genomic interval of approximately 103 kb was thus selected. Position 1 of this ~103 kb interval corresponds to position 798,334 in GenBank Accession number NT_001039.

In the next step, the selected 103 kb genomic interval was compared with known high-complexity repeat sequence family members or consensus sequences that are aligned with the test genomic sequences (SEQ ID Nos. 1-428) and all combinations of low-complexity tandem repeat sequences of at least 17 nucleotides in length (mono-, di-, tri-, and tetranucleotide units) known to be present in the human genome (SEQ ID Nos. 447-479). This comparison was done using the publicly available CENSOR program which can be found at the Genetic Information Research Institute website (girinst.org). This program utilizes the Smith-Waterman global alignment comparison algorithm to determine the locations and distribution of repeat sequences within the genomic interval. A Smith-Waterman alignment of repetitive with genomic sequences was performed with the following parameters: Length of margin sequence: 50 nt, minimum length to extract insertion: 12 nt, minimum margin to combine matching fragments: 30, similarity threshold: 22, similarity threshold to always keep match: 35, ratio threshold: 2.8, relative similarity threshold: 2.8, gap constant D1: 2.95, gap constant D2: 1.90, and mismatch penalty: -1.0. This analysis generated the following table, which

details the coordinates of repetitive sequence family members found in and adjacent to the human HIRA gene coding sequence.

Please delete the paragraph which begins at page 37, line 19 and replace it with the following paragraph:

In principle, the present method can be utilized to design, develop and produce single-copy genomic probes for any genomic interval where the DNA sequence is available and where a comprehensive set of repetitive sequence elements in the genome has been cataloged. Such catalogs are currently available for genomes for the following organisms (girinst.org): *Homo sapiens, Mus musculus, Arabidopsis thaliana, Canorhabditis elegans, Drosophila melanogaster, and Danio rerio.*

Please delete the paragraph which begins at page 38, line 5, with the following paragraph:

The locations of single copy probe sequences are determined directly from long contiguous genomic DNA sequences. The locations were determined by software that aligns the sequences of repetitive sequence family members with the target genomic sequence. Comparison of the target sequence with previously determined sequences of repetitive family members served to identify and delineate the bounds of repetitive elements within the target. The computer program, RepeatMasker (genome.washing-ton.edu/RM/RepeatMasker.html); Smit A.F.A. & Green

P., unpublished results), was used to determine the locations of repetitive sequence families in contiguous genomic sequences, usually ~100 kb in length. RepeatMasker compares a genomic sequence with a compilation of repetitive sequence families present in multiple copies in the human genome. This repeat sequence database contains representative and consensus sequences for the majority of human repetitive sequence families. The database can be expanded by addition of newly discovered repetitive sequence families (as shown in Example 6).

Please delete the first full paragraph of Example 6, and replace it with the following paragraph:

The increasing availability of accurate draft human genome sequences has facilitated development of single copy probes in accordance with the invention for many previously inaccessible chromosomal regions. Although the most current comprehensive up-to-date sequence databases have been used to detect repetitive elements (girinst.org/repbase) present in these draft sequences, hybridization of single copy probes to metaphase chromosomes has revealed that several probes contain previously unrecognized repetitive sequences. This was determined by documenting hybridization of a probe to the homologous chromosomal band where it is known to be mapped as well as other locations not found in the draft genome sequence.

Please delete the paragraph beginning at page 15, line 6 and replace it with the following paragraph:

> However, in order to optimize the yield and kinetics of the PCR reaction, the desired primer sequences are also subject to other criteria. First, a primer sequence should not be substantially self-complementary or complementary to the second primer. In particular, potential primer sequences are excluded which could result in the formation of stable hybrids involving the 3' terminus of the primer and either another sequence in the same or the second primer (defined as ≥6 base pairs). Additionally, the T_m of one member of the primer pair should occur within 2°C of its counterpart, which enables them to denature and anneal to the template nearly simultaneously. Software is well known in the art to identify primer sequences that satisfy all of the preferred criteria (see for example genome.wi.mit.edu/ftp/pub/software/primer.0.5/ or oligo.net/Oligo_6_tour.htm).

Please add the following paragraph in after the heading "BRIEF DESCRIPTION OF THE DRAWINGS" on page 5:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawings will be provided by the Office upon request and payment of the necessary fee.